

Letter to the Editor: Preparative Regimens in Acute Leukemia

Kamani et al. [1] report their experience of using total body irradiation followed by ARA-C for 20 children with acute leukemia undergoing BMT from matched sibling donors. Unfortunately, we are not able to assess the impact of this preparative regimen because data on the disease status of the patients are lacking. From reading the paper carefully, I think that 8 ALL patients relapsed on or within 3 months off-treatment; 4 had relapsed 3 or more months off-treatment and 2 had not relapsed; 5 of the 6 AML patients had not relapsed. I think that 5 of the 6 AML and 12 of the 14 ALL patients were in remission, either CR 1 or 2, but it is not easy to glean this information. An extra column in the table would have made the situation clearer. This information is vital, since we know that the risk of relapse post-BMT is directly related to the disease status pre-BMT.

Like Kamani, we have been influenced by the report of Brochstein et al. [2] Since 1991, all patients with ALL undergoing BMT at our centre have been prepared with 1,320 cGy of TBI (given as 8 fractions over 4 days) followed by 2 days of cyclophosphamide, 60 mg/kg/day. Of 23 patients undergoing allogeneic BMT (16 matched siblings), one suffered an early toxic death. One of 15 patients transplanted in CR1 or CR2 has relapsed, although our follow-up is of course much shorter than the patients reported by Kamani et al. [1] Does this mean our results are as good as, better, or worse than Kamani et al.'s?

Many reviews have pointed out the difficulties of comparing preparative regimens. [3] In 1985, Santos et al. [4] reported the use of busulphan/cyclophosphamide for patients, predominantly with AML. Since that time, BuCy has been a widely used alternative to TBI/Cy. However, recent randomised trials have demonstrated the inferiority of BuCy to TBI containing regimens, mainly in AML. As reviewed by Shank [5] these trials do not support the routine use of BuCy for AML, although BuCy is widely used for this indication.

Reports such as that of Kamani et al. [1] provide valuable pilot information on the use of various preparative regimens for BMT. Surely the reason that, for example, Miami Children's Hospital has adopted TBI/ARA-C for ALL is not this report, but the absence of a suitable randomized

trial. I believe the 10 years of reports of BuCy in AML should tell us that we should all be participating in prospective randomized trials of such preparative regimens.

The International Bone Marrow Transplant Registry has recently moved from retrospective data collection, and initiated a randomised trial of conditioning regimens in Severe Aplastic Anemia. At the last European Blood and Marrow Transplant Meeting in March 1995, a Paediatric Working Party was convened under the Chairmanship of Prof. Niethammer. The enthusiasm of the group should ensure that preparative regimens are an area explored in some of the studies being planned. Surely in 1995, we can learn from the past, and expect that in an international group, preparative regimens only be explored as part of prospective randomized trials.

Peter Shaw
Oncology Unit
The Children's Hospital
Sydney NSW 2050
Australia

REFERENCES

1. Kamani N, Bayever E, August CS, Bunin N, Goldwein JW, D'Angio GJ: Fractionated total-body irradiation preceding high-dose cytosine arabinoside as a preparative regimen for bone marrow transplantation in children with acute leukemia. *Med Pediatr Oncol* 25:179-184, 1995.
2. Brochstein JA, Kernan NA, Groshen S, Cirincione C, Shank B, Emanuel D, Laver J, O'Reilly RJ: Allogeneic bone marrow transplantation after hyperfractionated total-body irradiation and cyclophosphamide in children with acute leukemia. *N Engl J Med* 317:1618-1624, 1987.
3. Aurer I, Gale RP: Are new conditioning regimens for transplants in acute myelogenous leukemia better? *Bone Marrow Transplant* 7:255-261, 1991.
4. Santos GW, Tutschka PJ, Brookmeyer R, Saral R, Beschoner WE, Bias WB, Braine HG, Burns WH, Elfenbein GJ, Kaizer H, Mellits D, Sensenbrenner LL, Stuart RK, Yeager AM: Marrow transplantation for acute nonlymphocytic leukemia after treatment with busulfan and cyclophosphamide. *N Engl J Med* 309:1347-1353, 1983.
5. Shank B: Can total body irradiation be supplanted by busulfan in cytoreductive regimens for bone marrow transplantation? *Int J Radiation Oncology Biol Phys* 31:195-196, 1995.

Received October 2, 1995; accepted January 23, 1996.